

## SEQUENCE LISTING

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<110> Ponath, Paul D.
     Ringler, Douglas J.
     Jones, S. Tarran
     Newman, Walter
     Saldanha, Jose
     Bendig, Mary M.
<120> Humanized Immunoglobulin Reactive with
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<130> 1855.1017-000
<140> 08/700,737
<141> 1996-08-15
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             aggtccaact gcagcagcct ggggctgagc
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 aagcagaggc ctggacaagg
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                         caagggcaag
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                                     tctgaggact
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 acagcctaca
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                                                             cacctcagtc
                                                 ggggtcaagg
                                     attgactact
  agagggggtt acgacggatg
                         ggactatgct
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494

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qnngaagctt ggga
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Val His Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys
Pro Gly Thr Ser Val Lys Leu Ser Cys Lys Gly Tyr Gly Tyr Thr Phe
                             40
Thr Ser Tyr Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu
                         55
Glu Trp Ile Gly Glu Ile Asp Pro Ser Glu Ser Asn Thr Asn Tyr Asn
                                         75
                     70
 Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Ile Ser Ser Ser
                                     90
                 85
 Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val
                                                     110
                                 105
             100
 Tyr Tyr Cys Ala Arg Gly Gly Tyr Asp Gly Trp Asp Tyr Ala Ile Asp
                                                 125
                             120
 Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr
                         135
     130
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                     Met Gly Trp Ser Tyr Ile Ile Phe Phe Leu Val
 tca aca gct aca agt gtc cac tcc cag gtc caa ctg cag cag cct ggg
                                                                     98
 Ser Thr Ala Thr Ser Val His Ser Gln Val Gln Leu Gln Gln Pro Gly
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gct gag ctt gtg aag cct ggg act tca gtg aag ctg tcc tgc aag ggt Ala Glu Leu Val Lys Pro Gly Thr Ser Val Lys Leu Ser Cys Lys Gly 30 35 40	146
tat ggc tac acc ttc acc agc tac tgg atg cac tgg gtg aag cag agg Tyr Gly Tyr Thr Phe Thr Ser Tyr Trp Met His Trp Val Lys Gln Arg 45	194
cct gga caa ggc ctt gag tgg atc gga gag att gat cct tct gag agt Pro Gly Gln Gly Leu Glu Trp Ile Gly Glu Ile Asp Pro Ser Glu Ser 60 65 70 75	242
aat act aac tac aat caa aaa ttc aag ggc aag gcc aca ttg act gta Asn Thr Asn Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val 80 85	290
gac att tcc tcc agc aca gcc tac atg cag ctc agc agc ctg aca tct Asp Ile Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser 95 100 105	338
gag gac tct gcg gtc tac tat tgt gca aga ggg ggt tac gac gga tgg Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Gly Gly Tyr Asp Gly Trp 110 115	386
gac tat gct att gac tac tgg ggt caa ggc aca tca gtc acc Asp Tyr Ala Ile Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr 135	428
<210> 4 <211> 137 <212> PRT <213> Unknown	
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Pro Gly Thr Ser Val Lys Leu Ser Cys Lys Gly Tyr Gly Tyr Thr File	
Thr Ser Tyr Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu 55 60	
50 Glu Trp Ile Gly Glu Ile Asp Pro Ser Glu Ser Asn Thr Asn Tyr Asn 70 75 80	
65 Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Ile Ser Ser Ser 90 95.	
Gar Lou Thr Ser Glu Asp Ser Ala Val	
Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val	
Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Strain 110  100  Tyr Tyr Cys Ala Arg Gly Gly Tyr Asp Gly Trp Asp Tyr Ala Ile Asp 115  Tyr Trp Gly Gln Gly Thr Ser Val Thr	

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                 Met Lys Leu Pro Val Arg Leu Leu Val Leu Leu Leu
ttc tgg att cct gtt tcc gga ggt gat gtt gtg gtg act caa act cca
                                                                    99
Phe Trp Ile Pro Val Ser Gly Gly Asp Val Val Val Thr Gln Thr Pro
          15
ctc tcc ctg cct gtc agc ttt gga gat caa gtt tct atc tct tgc agg
Leu Ser Leu Pro Val Ser Phe Gly Asp Gln Val Ser Ile Ser Cys Arg
      30
 tot agt cag agt ctt gca aag agt tat ggg aac acc tat ttg tot tgg
                                                                    195
 Ser Ser Gln Ser Leu Ala Lys Ser Tyr Gly Asn Thr Tyr Leu Ser Trp
  45
 tac ctg cac aag cct ggc cag tct cca cag ctc ctc atc tat ggg att
                                                                    243
 Tyr Leu His Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Gly Ile
 tcc aac aga ttt tct ggg gtg cca gac agg ttc agt ggc agt ggt tca
                                                                     291
 Ser Asn Arg Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
 ggg aca gat ttc aca ctc aag atc agc aca ata aag cct gag gac ttg
                                                                     339
 Gly Thr Asp Phe Thr Leu Lys Ile Ser Thr Ile Lys Pro Glu Asp Leu
                              100
           95
 gga atg tat tac tgc tta caa ggt aca cat cag ccg tac acg ttc gga
                                                                     387
 Gly Met Tyr Tyr Cys Leu Gln Gly Thr His Gln Pro Tyr Thr Phe Gly
                          115
 ggg ggg acc aag ctg gaa ata aaa cgg gct gat gct gca cca act gta
                                                                     435
  Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala Pro Thr Val
                      130
  125
  tccatcttcc caccatccag taagcttggg aatccatatg actagtagat cctctagagt 495
  cgacctgcag gcatgcaagc ttccctatag tgagtcgtat
  <210> 6
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  <212> PRT
  <213> Artificial Sequence
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Met Lys Leu Pro Val Arg Leu Leu Val Leu Leu Phe Trp Ile Pro
Val Ser Gly Gly Asp Val Val Thr Gln Thr Pro Leu Ser Leu Pro
                                25
Val Ser Phe Gly Asp Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser
           20
                                               45
                            40
Leu Ala Lys Ser Tyr Gly Asn Thr Tyr Leu Ser Trp Tyr Leu His Lys
Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe
                        55
                                       75
                    70
Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                                    90
               85
Thr Leu Lys Ile Ser Thr Ile Lys Pro Glu Asp Leu Gly Met Tyr Tyr
                               105
            100
Cys Leu Gln Gly Thr His Gln Pro Tyr Thr Phe Gly Gly Thr Lys
                           120
Leu Glu Ile Lys Arg Ala Asp Ala Ala Pro Thr Val
                        135
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 Asp Val Val Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Phe Gly
                                    10
 Asp Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Ala Lys Ser
                 5
                                 25
 Tyr Gly Asn Thr Tyr Leu Ser Trp Tyr Leu His Lys Pro Gly Gln Ser
                                                45
                             40
 Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro
                                             60
                         55
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
                                         75
 Ser Thr Ile Lys Pro Glu Asp Leu Gly Met Tyr Tyr Cys Leu Gln Gly
                                     90
 Thr His Gln Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 <210> 8
 <211> 112
 <212> PRT
 <213> Homo sapiens
 Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 <400> 8
                                     10
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
                                 25
  Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
             20
                             40
          35
```

```
Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
                                    90
              85
Leu Gln Thr Pro Gln Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
                                105
<210> 9
<211> 121
<212> PRT
<213> Unknown
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<223> Mouse
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Thr
                                    10
Ser Val Lys Leu Ser Cys Lys Gly Tyr Gly Tyr Thr Phe Thr Ser Tyr
                                25
Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
                            40
Gly Glu Ile Asp Pro Ser Glu Ser Asn Thr Asn Tyr Asn Gln Lys Phe
                                             60
                       55
 Lys Gly Lys Ala Thr Leu Thr Val Asp Ile Ser Ser Ser Thr Ala Tyr
                                         75
                    70
 Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                                     90
                85
 Ala Arg Gly Gly Tyr Asp Gly Trp Asp Tyr Ala Ile Asp Tyr Trp Gly
                                 105
            100
 Gln Gly Thr Ser Val Thr Val Ser Ser
                             120
 <210> 10
 <211> 119
 <212> PRT
 <213> Homo sapiens
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 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
                                     10
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
 Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe
                          55
 Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
                                          75
                      70
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
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90

Ala Arg Gly Gly Tyr Tyr Gly Ser Gly Ser Asn Tyr Trp Gly Gln Gly 105

Thr Leu Val Thr Val Ser Ser 115

100

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                                                                   48
Met Lys Leu Pro Val Arg Leu Leu Val Leu Leu Phe Trp Ile Pro
gtt tcc gga ggt gat gtt gtg gtg act caa act cca ctc tcc ctg cct
                                                                   96
Val Ser Gly Gly Asp Val Val Thr Gln Thr Pro Leu Ser Leu Pro
             20
gtc agc ttt gga gat caa gtt tct atc tct tgc agg tct agt cag agt
                                                                   144
Val Ser Phe Gly Asp Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser
         35
ctt gca aag agt tat ggg aac acc tat ttg tct tgg tac ctg cac aag
Leu Ala Lys Ser Tyr Gly Asn Thr Tyr Leu Ser Trp Tyr Leu His Lys
                          55
     50
cet ggc cag tet eca cag etc etc atc tat ggg att tec aac aga ttt
Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe
                      70
 65
tot ggg gtg coa gac agg tto agt ggc agt ggt toa ggg aca gat tto
Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                  85
aca ctc aag atc agc aca ata aag cct gag gac ttg gga atg tat tac
Thr Leu Lys Ile Ser Thr Ile Lys Pro Glu Asp Leu Gly Met Tyr Tyr
            100
tgc tta caa ggt aca cat cag ccg tac acg ttc gga ggg ggg acc aag
                                                                    384
Cys Leu Gln Gly Thr His Gln Pro Tyr Thr Phe Gly Gly Gly Thr Lys
        115
                                                                    396
ctq gaa ata aaa
Leu Glu Ile Lys
    130
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 <223> Mouse
 <400> 12
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                                    10
Val Ser Gly Gly Asp Val Val Thr Gln Thr Pro Leu Ser Leu Pro
                                25
            20
Val Ser Phe Gly Asp Gln Val Ser Ile Ser Cys Arg Ser Ser Gln Ser
                            40
Leu Ala Lys Ser Tyr Gly Asn Thr Tyr Leu Ser Trp Tyr Leu His Lys
                                            60
                        55
Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe
                                        75
                    70
Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                                    90
                85
Thr Leu Lys Ile Ser Thr Ile Lys Pro Glu Asp Leu Gly Met Tyr Tyr
                                105
Cys Leu Gln Gly Thr His Gln Pro Tyr Thr Phe Gly Gly Gly Thr Lys
                                                 125
                            120
Leu Glu Ile Lys
    130
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<212> DNA
<213> Homo sapiens
<400> 13
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atctcctgca ggtctagtca gagcctcctc catagtaatg gatcaaacta tttggattgg 120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 180
teeggggtee etgacaggtt eagtggeagt ggateaggea cagattttae actgaaaate 240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct accaactcct 300
cagacgttcg gccaagggac caaggtggaa atcaaa
<210> 14
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      with a signal peptide sequence
 <221> CDS
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atg gga tgg agc tgt atc atc ctc ttc ttg gta tca aca gct aca agt
                                                                    48
 Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ser Thr Ala Thr Ser
                                      10
 gtc cac tcc cag gtc caa ctg cag cag cct ggg gct gag ctt gtg aag
                                                                    96
 Val His Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys
                                  25
 cct ggg act tca gtg aag ctg tcc tgc aag ggt tat ggc tac acc ttc
                                                                    144
 Pro Gly Thr Ser Val Lys Leu Ser Cys Lys Gly Tyr Gly Tyr Thr Phe
          35
                              40
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acc agc tac tgg atg cac tgg gtg aag cag agg cct gga caa ggc ctt
Thr Ser Tyr Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu
                         55
gag tgg atc gga gag att gat cct tct gag agt aat act aac tac aat
Glu Trp Ile Gly Glu Ile Asp Pro Ser Glu Ser Asn Thr Asn Tyr Asn
                     70
 65
caa aaa ttc aag ggc aag gcc aca ttg act gta gac att tcc tcc agc
                                                                   288
Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Ile Ser Ser
                 85
aca gcc tac atg cag ctc agc agc ctg aca tct gag gac tct gcg gtc
                                                                    336
Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val
                                 105
            100
tac tat tgt gca aga ggg ggt tac gac gga tgg gac tat gct att gac
                                                                    384
Tyr Tyr Cys Ala Arg Gly Gly Tyr Asp Gly Trp Asp Tyr Ala Ile Asp
                             120
        115
                                                                    420
tac tgg ggt caa ggc acc tca gtc acc gtc tcc tca
Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
                         135
    130
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 <223> Mouse Act-1 antibody heavy chain variable region
       with a signal peptide sequence
 Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ser Thr Ala Thr Ser
 <400> 15
                                     10
 Val His Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys
                                  25
 Pro Gly Thr Ser Val Lys Leu Ser Cys Lys Gly Tyr Gly Tyr Thr Phe
 Thr Ser Tyr Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu
                          55
 Glu Trp Ile Gly Glu Ile Asp Pro Ser Glu Ser Asn Thr Asn Tyr Asn
                                          75
                      70
 Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Ile Ser Ser Ser
                                      90
                  85
 Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val
                                  105
             100
 Tyr Tyr Cys Ala Arg Gly Gly Tyr Asp Gly Trp Asp Tyr Ala Ile Asp
                                                  125
                              120
         115
 Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
                          135
      130
  <210> 16
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  <213> Artificial Sequence
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      region with a signal peptide sequence
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Met Glu Phe Gly Leu Ser Trp Leu Phe Leu Val Ala Ile Leu Lys Gly
gtc cag tgt cag gtg cag ctt gtg cag tct ggg gct gag gtg aag aag
Val Gln Cys Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
cct ggg gcc tca gtg aag gtt tcc tgc aag gct tct gga tac acc ttc
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
act agc tat gct atg cat tgg gtg cgc cag gcc ccc gga caa agg ctt
                                                                   192
Thr Ser Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu
gag tgg atg gga tgg atc aac gct ggc aat ggt aac aca aaa tat tca
                                                                    240
Glu Trp Met Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser
                                          75
cag aag ttc cag ggc aga gtc acc att acc agg gac aca tcc gcg agc
                                                                    288
Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser
aca gcc tac atg gag ctg agc agc ctg aga tct gaa gac acg gct gtg
                                                                    336
Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
                                 105
tat tac tgt gcg aga gga ggt tac tat ggt tcg ggg agc aac tac tgg
                                                                    384
Tyr Tyr Cys Ala Arg Gly Gly Tyr Tyr Gly Ser Gly Ser Asn Tyr Trp
                             120
                                                                    414
ggc cag gga acc ctg gtc acc gtc tcc tca
Gly Gln Gly Thr Leu Val Thr Val Ser Ser
                         135
<210> 17
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 <223> Human 21/28'CL antibody heavy chain variable
       region with a signal peptide sequence
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                                     10
 Val Gln Cys Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
                                 25
             20
```

```
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
                            40
Thr Ser Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu
                        55
Glu Trp Met Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser
                                        75
Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser
                                     90
Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
                                105
Tyr Tyr Cys Ala Arg Gly Gly Tyr Tyr Gly Ser Gly Ser Asn Tyr Trp
                            120
        115
Gly Gln Gly Thr Leu Val Thr Val Ser Ser
                        135
<210> 18
<211> 540
<212> DNA
<213> Artificial Sequence
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<223> Portion of humanized Act-1 antibody heavy chain
      with a heavy chain signal peptide sequence
<221> CDS
<222> (1)...(540)
atg aaa tgc acc tgg gtc att ctc ttc ttg gta tca aca gct aca agt
Met Lys Cys Thr Trp Val Ile Leu Phe Leu Val Ser Thr Ala Thr Ser
 1
gtc cac tcc cag gtc caa cta gtg cag tct ggg gct gag gtt aag aag
                                                                   96
Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
             20
cct ggg gct tca gtg aag gtg tcc tgc aag ggt tct ggc tac acc ttc
                                                                   144
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Gly Ser Gly Tyr Thr Phe
                                                  45
         35
acc agc tac tgg atg cat tgg gtg agg cag gcg cct ggc caa cgt cta
                                                                   192
Thr Ser Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu
     50
                         55
gag tgg atc gga gag att gat cct tct gag agt aat act aac tac aat
                                                                   240
Glu Trp Ile Gly Glu Ile Asp Pro Ser Glu Ser Asn Thr Asn Tyr Asn
                     70
                                          75
 65
caa aaa ttc aag gga cgc gtc aca ttg act gta gac att tcc gct agc
                                                                   288
Gln Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Ile Ser Ala Ser
                 85
aca gcc tac atg gag ctc agc agc ctg aga tct gag gac act gcg gtc
Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
                                105
            100
```

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tac tat tgt gca aga ggg ggt tac gac gga tgg gac tat gct att gac
                                                                   384
Tyr Tyr Cys Ala Arg Gly Gly Tyr Asp Gly Trp Asp Tyr Ala Ile Asp
                            120
        115
tac tgg ggt caa ggc acc ctg gtc acc gtc tcc tca gcc tcc acc aag
                                                                    432
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
                                             140
                        135
    130
ggc cca tcg gtc ttc ccc ctg gca ccc tcc tcc aag agc acc tct ggg
                                                                    480
Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
                                         155
                    150
145
ggc aca geg gec etg ggc tgc etg gtc aag gac tac ttc eec gaa eeg
                                                                    528
Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
                                     170
                165
                                                                    540
gtg acg gtg tcg
Val Thr Val Ser
            180
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<223> Portion of humanized Act-1 antibody heavy chain
      with a heavy chain signal peptide sequence
Met Lys Cys Thr Trp Val Ile Leu Phe Leu Val Ser Thr Ala Thr Ser
                                     10
Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
                                 25
 Pro Gly Ala Ser Val Lys Val Ser Cys Lys Gly Ser Gly Tyr Thr Phe
                                                  45
                             40
 Thr Ser Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu
                                              60
                         55
Glu Trp Ile Gly Glu Ile Asp Pro Ser Glu Ser Asn Thr Asn Tyr Asn
                                          75
                     70
 Gln Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Ile Ser Ala Ser
                                     90
                 85
 Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
                                                      110
                                  105
             100
 Tyr Tyr Cys Ala Arg Gly Gly Tyr Asp Gly Trp Asp Tyr Ala Ile Asp
                                                  125
                             120
         115
 Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
                                              140
                          135
     130
 Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
                                          155
                     150
 Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
                                      170
                 165
 Val Thr Val Ser
             180
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<210> 20 <211> 413

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<212> DNA
<213> Artificial Sequence
<220>
<223> Portion of humanized Act-1 antibody light chain
      with a light chain signal peptide sequence
<400> 20
atgaagttgc ctgttaggct gttggtgctt ctgttgttct ggattcctgt ttccggaggt 60
gatgttgtga tgactcaaag tccactctcc ctgcctgtca cccctggaga accagcttct 120
atctcttgca ggtctagtca gagtcttgca aagagttatg ggaacaccta tttgtcttgg 180
tacctgcaga agcctggcca gtctccacag ctcctcatct atgggatttc caacagattt 240
tetggggtge cagacaggtt cagtggeagt ggtteaggga cagattteae acteaagate 300
tcgcgagtag aggctgagga cgtgggagtg tattactgct tacaaggtac acatcagccg 360
tacacgttcg gacaggggac caaggtggaa ataaaacggg ctgatgcggc gcc
<210> 21
<211> 138
<212> PRT
<213> Artificial Sequence
<220>
<223> Portion of humanized Act-1 antibody light chain
      with a light chain signal peptide sequence
<400> 21
Met Lys Leu Pro Val Arg Leu Leu Val Leu Leu Phe Trp Ile Pro
                                     10
Val Ser Gly Gly Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro
                                 25
            20
Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
                             40
Leu Ala Lys Ser Tyr Gly Asn Thr Tyr Leu Ser Trp Tyr Leu Gln Lys
                                             60
    50
                         55
Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe
                                         75
Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
                                     90
                85
Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr
                                 105
Cys Leu Gln Gly Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys
                             120
        115
Val Glu Ile Lys Arg Ala Asp Ala Ala Pro
    130
                         135
<210> 22
<211> 94
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
 <400> 22
tttccggagg tgatgttgtg atgactcaaa gtccactctc cctgcctgtc acccctggag 60
aaccagette tatetettge aggtetagte agag
```

```
<211> 94
<212> DNA
<213> Artificial Sequence
<223> Synthetic oligonucleotide
<400> 23
actggccagg cttctgcagg taccaagaca aataggtgtt cccataactc tttgcaagac 60
tctgactaga cctgcaagag atagaagctg gttc
<210> 24
<211> 83
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
<400> 24
cetggccagt ctccacaget cetcatetat gggattteca acagatttte tggggtgcca 60
gacaggttca gtggcagtgg ttc
<210> 25
<211> 84
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
<400> 25
actcgcgaga tcttgagtgt gaaatctgtc cctgaaccac tgccactgaa cctgtctggc 60
accccagaaa atctgttgga aatc
<210> 26
<211> 67
<212> DNA
<213> Artificial Sequence
<223> Synthetic oligonucleotide
<400> 26
tctcgcgagt agaggctgag gacgtgggag tgtattactg cttacaaggt acacatcagc 60
                                                                    67
cgtacac
<210> 27
<211> 86
 <212> DNA
<213> Artificial Sequence
 <223> Synthetic oligonucleotide
 <400> 27
atggcgccgc atcagcccgt tttatttcca ccttggtccc ctgtccgaac gtgtacggct 60
                                                                     86
gatgtgtacc ttgtaagcag taatac
```

```
<210> 28
<211> 93
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
<400> 28
ataagcttcg ccatgaaatg cacctgggtc attetettet tggtatcaac agetacaagt 60
gtccactccc aggtccaact agtgcaccgg tta
<210> 29
<211> 93
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
<400> 29
taaccggtgc actagttgga cctgggagtg gacacttgta gctgttgata ccaagaagag 60
aatgacccag gtgcatttca tggcgaagct tat
<210> 30
<211> 87
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
<400> 30
caactagtgc agtctggggc tgaggttaag aagcctgggg cttcagtgaa ggtgtcctgc 60
aagggttctg gctacacctt caccagc
 <210> 31
 <211> 88
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Synthetic oligonucleotide
 taaccggtac tctagacgtt ggccaggcgc ctgcctcacc caatgcatcc agtagctggt 60
 <400> 31
 gaaggtgtag ccagaaccct tgcaggac
 <210> 32
 <211> 76
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Synthetic oligonucleotide
 cgtctagagt ggatcggaga gattgatcct tctgagagta atactaacta caatcaaaaa 60
 ttcaagggac gcgtca
```

```
<210> 33
<211> 76
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
taaccggtgt gctagcggaa atgtctacag tcaatgtgac gcgtcccttg aatttttgat 60
tgtagttagt attact
<210> 34
<211> 88
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
<400> 34
ccgctagcac agcctacatg gagctcagca gcctgagatc tgaggacact gcggtctact 60
attgtgcaag agggggttac gacggatg
<210> 35
<211> 88
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
tcaccggtgc ggtgaccagg gtgccttgac cccagtagtc aatagcatag tcccatccgt 60
cgtaaccccc tcttgcacaa tagtagac
 <210> 36
 <211> 85
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Synthetic oligonucleotide
 <400> 36
 ctggtcaccg tctcctcagc ctccaccaag ggcccatcgg tcttccccct ggcaccctcc 60
 tccaagagca cctctggggg cacag
 <210> 37
 <211> 85
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Synthetic oligonucleotide
 tcaccggttc ggggaagtag tccttgacca ggcagcccag ggccgctgtg cccccagagg 60
 tgctcttgga ggagggtgcc agggg
```

<210> 38 <211> 10 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 38 ctggccaacg	10
<210> 39 <211> 34 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 39 cacattgact gtagacactt ccgctagcac agcc	34
<210> 40 <211> 24 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 40 ccggaggtga tgttgtggtg actc	24
<210> 41 <211> 24 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 41 taagcttccg ccatgggatg gagc	24
<210> 42 <211> 25 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 42 ggtgacacta gtgccttgac cccag	25
<210> 43 <211> 24 <212> DNA <213> Artificial Sequence	

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<223> Synthetic oligonucleotide
<400> 43
                                                                    24
taagcttccg ccatgaagtt gcct
<210> 44
<211> 21
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
<400> 44
                                                                    21
ggcgccgcat cagcccgttt t
<210> 45
<211> 20
<212> DNA
<213> Artificial Sequence
<223> Synthetic oligonucleotide
<400> 45
                                                                     20
cggcgccatc tgtcttcatc
<210> 46
<211> 18
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
 <400> 46
                                                                     18
aagcttctaa cactctcc
 <210> 47
 <211> 19
 <212> PRT
 <213> Unknown
 <220>
 <223> Mouse
 Asp Val Val Val Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Phe Asp
                                      10
 1
 Gly Gln Val
 <210> 48
 <211> 11
 <212> PRT
 <213> Unknown
```

```
<220>
<223> Mouse
<400> 48
Asp Val Val Val Thr Gln Thr Pro Leu Ser Leu
            5
<210> 49
<211> 8
<212> PRT
<213> Unknown
<220>
<223> Mouse
<400> 49
Asp Tyr Ala Ile Asp Tyr Trp Gly
                 5
 1
<210> 50
<211> 113
<212> PRT
<213> Artificial Sequence
 <223> Mouse consensus sequence
 Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
                                     10
 Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
                 5
                                 25
 Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
                             40
 Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
                                              60
                         55
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
                     70
 Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
                                      90
 Thr His Val Pro Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
 Lys
  <210> 51
  <211> 114
  <212> PRT
  <213> Artificial Sequence
  <220>
  <223> Human consensus sequence
  <221> UNSURE
  <222> (33)...(33)
  <223> Xaa = Any Amino Acid
```

```
<221> UNSURE
<222> (100) ... (100)
<223> Xaa = Any Amino Acid
<221> UNSURE
<222> (103)...(103)
<223> Xaa = Any Amino Acid
<400> 51
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
                                    10
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
                                25
            20
Xaa Asp Gly Asn Asn Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln
                                                 45
                            40
Ser Pro Gln Leu Leu Ile Tyr Leu Val Ser Asn Arg Ala Ser Gly Val
                        55
Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys
                                         75
                    70
Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln
                                    90
                85
Ala Leu Gln Xaa Pro Arg Xaa Thr Phe Gly Gln Gly Thr Lys Val Glu
                                105
            100
Ile Lys
<210> 52
<211> 112
<212> PRT
<213> Artificial Sequence
<223> Reshaped humanized sequence
<400> 52
Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
                  5
 1
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Ala Lys Ser
                                 25
Tyr Gly Asn Thr Tyr Leu Ser Trp Tyr Leu Gln Lys Pro Gly Gln Ser
                             40
Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro
                                             60
                         55
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
                                         75
                     70
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Gly
                                     90
Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
             100
 <210> 53
 <211> 127
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> Mouse consensus sequence
```

```
<221> UNSURE
<222> (106) ... (107)
<223> Xaa = Any Amino Acid
<221> UNSURE
<222> (110)...(110)
<223> Xaa = Any Amino Acid
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
                                    10
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
                                25
Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
                            40
Gly Arg Ile Asp Pro Asn Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe
                                             60
                       55
Lys Ser Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
                                        75
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                                     90
                85
Ala Arg Tyr Tyr Gly Gly Ser Ser Xaa Xaa Val Tyr Xaa Tyr Trp
                                 105
Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
                            120
 <210> 54
 <211> 129
 <212> PRT
 <213> Artificial Sequence
 <223> Human consensus sequence
 <221> UNSURE
 <222> (115)...(115)
 <223> Xaa = Any Amino Acid
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
             20
 Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 Gly Trp Ile Asn Pro Tyr Gly Asn Gly Asp Thr Asn Tyr Ala Gln Lys
                          55
 Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala
                                          75
                     70
 Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr
                                      90
 Cys Ala Arg Ala Pro Gly Tyr Gly Ser Gly Gly Gly Cys Tyr Arg Gly
                                 105
  Asp Tyr Xaa Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
                              120
  Ser
```

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<210> 55
<211> 121
<212> PRT
<213> Artificial Sequence
<220>
<223> Reshaped humanized sequence
<400> 55
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
Ser Val Lys Val Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Ser Tyr
Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Ile
                            40
Gly Glu Ile Asp Pro Ser Glu Ser Asn Thr Asn Tyr Asn Gln Lys Phe
                                             60
                        55
Lys Gly Arg Val Thr Leu Thr Val Asp Ile Ser Ala Ser Thr Ala Tyr
                                         75
                   70
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                                     90
                85
Ala Arg Gly Gly Tyr Asp Gly Trp Asp Tyr Ala Ile Asp Tyr Trp Gly
                                 105
            100
Gln Gly Thr Leu Val Thr Val Ser Ser
        115
<210> 56
<211> 35
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic oligonucleotide
<221> modified base
 <222> (30) ... (30)
 <223> n = I
 <400> 56
                                                                    35
cccaagcttc cagggrccar kggataracn grtgg
 <210> 57
 <211> 32
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Synthetic oligonucleotide
                                                                    32
 cccaagctta cgaggggaa gacatttggg aa
 <210> 58
 <211> 34
 <212> DNA
 <213> Artificial Sequence
 <220>
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<223> Synthetic oligonucleotide	
<400> 58 gggaattcat graatgsasc tgggtywtyc tctt	34
<210> 59 <211> 33 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 59 actagtcgac atgaagwtgt ggbtraactg grt	33
<210> 60 <211> 30 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 60 cccaagctta ctggatggtg ggaagatgga	30
<210> 61 <211> 39 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 61 actagtcgac atggatttwc argtgcagat twtcagctt	39
<210> 62 <211> 32 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 62 ggaagettee accatggatt teggaetgge ee	32
<210> 63 <211> 27 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic oligonucleotide	
<400> 63 qqactagtgg tttggacgag cctgttg	27

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<210> 64
<211> 396
<212> DNA
<213> Unknown
<220>
<223> Mouse
ttttatttcc agcttggtcc cccctccgaa cgtgtacggc tgatgtgtac cttgtaagca 60
<400> 64
gtaatacatt cccaagtcct caggetttat tgtgctgate ttgagtgtga aatctgteec 120
tgaaccactg ccactgaacc tgtctggcac cccagaaaat ctgttggaaa tcccatagat 180
gaggagetgt ggagaetgge caggettgtg caggtaccaa gacaaatagg tgttcccata 240
actetttgca agactetgac tagacetgca agagatagaa acttgatete caaagetgac 300
aggcagggag agtggagttt gagtcaccac aacatcacct ccggaaacag gaatccagaa 360
caacagaagc accaacagcc taacaggcaa cttcat
<210> 65
<211> 336
<212> DNA
<213> Homo sapiens
<400> 65
tttgatttcc accttggtcc cttggccgaa cgtctgagga gttggtagag cttgcatgca 60
gtaataaacc ccaacatcct cagcctccac tctgctgatt ttctgtgtaa aatctgtgcc 120
tgatccactg ccactgaacc tgtcagggac cccggaggcc cgattagaac ccaaatagat 180
caggagetgt ggagaetgee etggettetg caggtaceaa tecaaatagt ttgatecatt 240
actatggagg aggetetgae tagacetgea ggagatggag geeggetete caggggtgae 300
gggcagggag agtggagact gagtcatcac aatatc
<210> 66
<211> 420
<212> DNA
 <213> Artificial Sequence
 <220>
 <223> Mouse Act-1 antibody heavy chain variable region
       with a signal peptide sequence-antisense
 <400> 66
 tgaggagacg gtgactgagg tgccttgacc ccagtagtca atagcatagt cccatccgtc 60
 gtaaccccct cttgcacaat agtagaccgc agagtcctca gatgtcaggc tgctgagctg 120
 catgtagget gtgctggagg aaatgtctac agtcaatgtg gccttgccct tgaatttttg 180
 attgtagtta gtattactct cagaaggatc aatctctccg atccactcaa ggccttgtcc 240
 aggectetge tteacceagt geatecagta getggtgaag gtgtagecat aaccettgea 300
 ggacagette actgaagtee caggetteac aageteagee ceaggetget geagttggac 360
 ctgggagtgg acacttgtag ctgttgatac caagaagagg atgatacagc tccatcccat 420
 <210> 67
 <211> 414
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Human 21/28'CL antibody heavy chain variable
       region with a signal peptide sequence-antisense
 <400> 67
```

## 25/25

tgaggagacg gtgaccagg tcctctcgca cagtaatac ggctgtgctc gcggatgtg ttttgtgtta ccattgcca ctggcgcacc caatgcata cttcactgag gccccaggc ctggacacct tttaaaata	a cageegtgte ceetggtaat g egttgateea g catagetagt t tetteacete	ttcagatctc ggtgactctg tcccatccac gaaggtgtat agccccagac	aggctgctca ccctggaact tcaagccttt ccagaagcct tgcacaagct	gctccatgta tctgtgaata gtccgggggc tgcaggaaac gcacctgaca	180 240 300
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Cttc.